REMARKS

Applicants respectfully request reconsideration of the rejections set forth in the Office Action mailed on June 25, 2004. Claims 85-91 have been cancelled herein without prejudice to pursuing their subject matter at a future time. Furthermore, no estoppels are intended by their cancellation. Accordingly, Claims 18, 19, 65, 67, 76, 82, and 84 remain pending.

The current claim cancellations have been made to better define one embodiment of the invention. None of the amendments to the claims is related to the statutory requirements of patentability unless expressly stated so herein. Applicants reserve the right to prosecute the originally filed claims in the future.

Rejections under 35 U.S.C. §112

Treatment of Cancer

Claims 18, 19, 65, 67, 76, 82 and 84 have been rejected under 35 U.S.C. §112, first paragraph, because the specification, while being enabling for the treatment of certain cancers, allegedly does not reasonably provide enablement for the treatment of cancer in general. Applicants disagree and traverse this rejection.

The National Cancer Institute has instituted protocols for determining the efficacy of compounds in treating cancer. Specifically, according to these protocols, therapeutic agents should be tested with the following cell lines: leukemia (e.g., L1210 and P388), melanoma (e.g., B16), lung carcinoma (e.g., LL) and carcinosarcoma (e.g., W256). *See* Cancer Chemotherapy Reports, Part 3, Vol. 3, No. 2, (1972). These protocols are currently considered to be standard practices for those of skill in the art.

Quinazolinone KSP inhibitors claimed herein have been shown to inhibit cell proliferation in human tumor cell lines of the following tumor types: lung (NCI-H460, A549), breast (MDA-MB-231, MCF-7, MCF-7/ADR-RES), colon (HT29, HCT15), ovarian (SKOV-3, OVCAR-3), leukemia (HL-60(TB), K-562), central nervous system (SF-268), renal (A498), osteosarcoma (U2-OS), and cervical (HeLa). In addition, a mouse tumor line (B16, melanoma) was also growth-inhibited in the presence of the quinazolinone compounds. See, PCT WO 01/98278. Applicants submit that the use of these cell lines to demonstrate efficacy for the

therapeutic agents claimed herein is consistent with the National Cancer Institute's protocols for testing.

Moreover, a compound claimed herein has been tested in Phase I human clinical trials. The Phase I trials were open-label, non-randomized, dose-finding trials designed to study the safety, tolerability, pharmacokinetic and pharmacodynamic profile of a compound as claimed herein. In total, 75 patients with multiple advanced solid tumors were enrolled and treated with SB-715992 in these trials. The more common tumor types were colon, renal cell carcinoma, sarcoma, breast and lung cancer. Prolonged disease stabilization, ranging from 16 to more than 32 weeks, was observed in 8 of 30 patients representing a variety of tumor types. *See* Gonzales et al. (2002) Proc Am. Assoc. Cancer Res., Abstr. 1337; Johnson et al. (2002) 93rd Annual Meeting of the American Association for Cancer Research, San Francisco, CA, 43; Burris et al. (2003) European Journal of Cancer Suppl. 1, S172; and Chu et al. (2003) Proc. Am. Assoc. Clin. Oncol. 22, 525.

A broad Phase II clinical trial program for one of the claimed compounds isongoing. The Phase II program includes non-small cell lung, breast, ovarian, colorectal, renal, head and neck, prostate, melanoma and hematological cancers. Some of these trials are jointly sponsored by the assignee of the present application and the National Cancer Institute.

Finally, the claims of the present invention encompass a limited number of compounds. The claimed compounds have a high degree of structural similarity. More specificially, each of the compounds is a quinazolinone amide.

Applicants submit that, given the limited number of compounds encompassed by the claims of the instant invention, the structural similarity between the claimed compounds, the broad spectrum of tumor cell lines examined, and the inhibitory effect of the compounds claimed herein on these cell lines, these test results fully support the claims directed towards the treatment of cancer. Accordingly, Applicants respectfully request that the rejection be withdrawn.

Methods of Inhibiting Mitosis

Claims 85-91 have been rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the enablement requirement. Applicants disagree. However, as the

claims have been cancelled herein, Applicants maintain that the rejection is moot and requests that the rejection be withdrawn.

Rejections under 35 U.S.C. §102

Claims 85-91 have been rejected under 35 U.S.C. §102(e) as being inherently anticipated by Baxter et al. U.S. Patent No. 6,545,005. As the claims have been cancelled herein, Applicants maintain that the rejection is moot and requests that the rejection be withdrawn.

Applicants respectfully maintain that all pending claims are in condition for allowance. Therefore, Applicants respectfully request a Notice of Allowance for this application from the Examiner. Should any unresolved issues remain, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

Please grant any extensions of time required to enter this reply, and charge any additional required fees to our Deposit Account No. 06-0916.

Respectfully submitted,

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Date: September 2, 2004

By: _____

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